



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCESOPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361MEMORANDUM

DATE: 08/26/09

SUBJECT: HED Review of, "Residential Hazard, Exposure and Risk Assessment for a New, Topical Ectoparasiticide for Dogs that Contains Fipronil, (S)-Methoprene and Amitraz"

PC Code: 106201

MRID No.: 477813-01

Petition No.: NA

Assessment Type: NA

TXR No.: NA

DP Barcode: 367277

Registration No.: NA

Regulatory Action: Data Evaluation Record

Reregistration Case No.: NA

CAS No.: 33089-61-1

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The purpose of this memorandum is to review and respond to the "white paper" document submitted by Merial Limited. The document, *Residential Hazard, Exposure and Risk Assessment for a New, Topical Ectoparasiticide for Dogs that Contains Fipronil, (S)-Methoprene and Amitraz (FLAC)*, was submitted by Merial due to a request by the Health Effects Division (HED). The Agency met with Merial Limited on April 14, 2009 to discuss a proposed top-spot pet product containing fipronil, (S)-methoprene and amitraz. Of particular interest to the HED was Merial's pet fur clipping residue transfer study with the active ingredient, amitraz. Specifically, the results of the fur clipping study and how these compared to

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residue transfer studies performed using the cotton glove petting (or stroking) method, as were done for fipronil and (S)-methoprene.

The following passage from an April 14, 2009 meeting between Merial Limited and the Agency describes HED's request for the white paper document and what it should entail: "Merial will submit a weight-of-evidence approach in a white paper showing that the clipping study data are comparable to the Frontline and FLAC cotton glove petting studies. The dermal absorption argument would also be submitted with the white paper. EPA agreed to review the white paper submission and provide comment. EPA will review the amitraz (pet fur) clipping data study as scheduled under PRJA. It was noted that the new dislodgeable residue studies include fipronil and (S)-methoprene data as well. Other data such as physico-chemical properties should be used as supporting data in the submission, including study summaries and comparison of study results (residue transfer)."

In the past, the Agency has typically required a stroking or petting study to determine the amount of pesticide residue available for transfer from the pet to the exposed individual. These studies were conducted using a bare or gloved hand and involved the petting or stroking of a defined area of the animal for either a specific number of repeated motions or for a pre-determined period of time. A measure of the residue transferred to hand was then determined by means of hand wash, if a bare hand, or by analysis of the glove. The resulting residue values were then either compared to the total amount of ai applied to the animal, resulting in a percent estimate of the amount anticipated to transfer or used directly as a measure of transferable residue (TR).

Since these petting/stroking studies involved human subjects who were directly exposed to a pesticide-treated animal, the Agency debated whether this implied intentional human exposure to a pesticide; which, under the Government-wide Common Rule (EPA 40 CFR 26 – Protection of Human Subjects) would not be allowable unless all appropriate criteria pertaining to ethical conduct of the studies were adhered to. Rather than advise Merial Limited to perform a study which could have later been determined unacceptable, HED recommended an alternative transfer study method, pet fur clipping. HED recognizes that the petting/stroking studies and pet fur clipping studies differ and, therefore, the resulting data is subject to interpretation due to the noted differences in the sampling method.

The Agency has reviewed the document submitted by Merial and finds the information provided useful for human health risk assessment characterization purposes. Merial has adequately presented a comparison of the amitraz fur clipping study and the fipronil and (S)-methoprene cotton glove petting study results. Based upon the data submitted and reviewed, HED is satisfied that the amitraz fur clipping study is an acceptable surrogate for an amitraz petting study and, likewise, represents the amount of active ingredient which is anticipated to be available to transfer to an individual contacting an animal treated with the amitraz-containing formulation. HED will review the amitraz pet fur clipping study as submitted under PRJA and, if deemed acceptable for quantitative risk assessment purposes, it will be used to estimate risk of individuals exposed to animals treated with the product.

HED cannot comment on the validity of the argument for a reduction in percent dermal absorption within this memorandum at this time; however, Merial's rationale is under

consideration. Further communication between HED and Merial will be required to fully address the issue.

Merial submitted a full risk assessment as a part of their white paper document. While this falls outside of HED's direction/request for the white paper submission, the methods used and details incorporated by Merial may prove useful when the proposed product undergoes the human health risk assessment. HED appreciates the additional effort exhibited by Merial Limited; however, it should be noted that HED's interpretation and use of the submitted pet fur clipping study and resulting human health risk assessment may differ from that presented in the white paper submission.